

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

10X GENOMICS, INC. and PRESIDENT
AND FELLOWS OF HARVARD
COLLEGE,

Plaintiffs,

v.

NANOSTRING TECHNOLOGIES, INC.,

Defendant.

C.A. No. 22-261 (MFK)

JURY TRIAL DEMANDED

NANOSTRING TECHNOLOGIES, INC.,

Counterclaim-Plaintiff,

v.

10X GENOMICS, INC.,

Counterclaim-Defendant.

**NANOSTRING TECHNOLOGIES, INC. FIRST AMENDED ANSWER, AFFIRMATIVE
DEFENSES, AND COUNTERCLAIMS TO PLAINTIFFS' FIRST AMENDED
COMPLAINT**

OF COUNSEL:

Edward R. Reines
Derek C. Walter
WEIL, GOTSHAL & MANGES LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
(650) 802-3000

FARNAN LLP
Brian E. Farnan (Bar No. 4089)
Michael J. Farnan (Bar No. 5165)
919 N. Market St., 12th Floor
Wilmington, DE 19801
(302) 777-0300
(302) 777-0301 (Fax)
bfarnan@farnanlaw.com
mfarnan@farnanlaw.com

*Attorneys for Defendant
Nanostring Technologies, Inc.*

Date: August 16, 2022

Defendant NanoString Technologies, Inc. (“NanoString”) hereby provides its Answer to the First Amended Complaint (“FAC”) of 10x Genomics, Inc. (“10x”) and President and Fellows of Harvard College (“Harvard”) (collectively “Plaintiffs”), and amended Counterclaim as against 10x (“Counterclaim-Defendant”) as set forth below. Unless expressly admitted, NanoString denies each and every allegation in Plaintiffs’ FAC. To the extent the allegations in the FAC purport to characterize the nature or contents of the Exhibits to the FAC, NanoString lacks sufficient knowledge or information to form a belief as to the truth of those allegations and on that basis denies them. Additionally, to the extent that the headings or any other non-numbered statements in the FAC contain any allegations, NanoString denies each and every such allegation.

NATURE OF THE ACTION

1. NanoString admits that the FAC purports to state a claim for patent infringement of United States Patent Nos. 10,227,639 (“the 639 Patent”), 11,021,737 (“the 737 Patent”), 11,293,051 (“the 051 Patent”), 11,293,052 (“the 052 Patent”), and 11,293,054 (“the 054 Patent”) (collectively, the “Asserted Patents”) arising under the patent laws of the United States, Title 35, United States Code, including 35 U.S.C. § 271. Except as so admitted, NanoString denies any remaining allegations in paragraph 1.

THE PARTIES

2. Admitted.

3. Denied.

4. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 4 and on that basis denies them.

5. NanoString admits that it is a Delaware Corporation with its principal place of business is located in Seattle, WA. Except as so admitted, NanoString denies any remaining allegations in paragraph 5.

6. Denied.

JURISDICTION AND VENUE

7. NanoString incorporates by reference and restates its responses to paragraphs 1-6 of the FAC as though fully set forth herein.

8. NanoString admits that the FAC purports to state a claim for patent infringement arising under the patent laws of the United States, 35 U.S.C. §§ 1, et seq., including in particular 35 U.S.C. §§ 271. NanoString further admits that this Court has subject matter jurisdiction over causes of action for alleged patent infringement pursuant to 28 U.S.C. §§ 1331 and 1338(a).

9. NanoString admits that it is an entity organized under the laws of Delaware and that venue is proper in this District. Except as so admitted, NanoString denies any remaining allegations of paragraph 9.

A. Response to Allegations Regarding 10x's Products

10. Denied.

11. Denied.

12. Denied.

13. Denied.

14. Denied.

B. Response To Allegations Regarding 10x and *In Situ* Technologies

15. Paragraph 15 of the FAC includes allegations that are vague, ambiguous, and incomplete, and on that basis NanoString denies the allegations of paragraph 15.

16. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 16 and on that basis denies them.

17. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 17 and on that basis denies them.

C. Response to Allegations Regarding NanoString's Products

18. NanoString admits that it announced the launch of its Technology Access Program for the Spatial Molecular Imager Platform in March 2021. NanoString further admits that it issued a press release referencing the new CosMx Spatial Molecular Imager in November 2021. NanoString admits that Paragraph 18 accurately quotes a portion of NanoString's website. Paragraph 18 of the FAC further includes allegations that purport to characterize technical aspects of NanoString's products in a manner that is vague, ambiguous, and incomplete, and on that basis NanoString denies the remaining allegations of paragraph 18.

19. Denied.

20. NanoString admits that it markets certain products under the trade name CosMx. Paragraph 20 of the FAC further includes allegations that purport to characterize technical aspects of NanoString's products in a manner that is vague, ambiguous, and incomplete, and on that basis NanoString denies the remaining allegations of paragraph 20.

D. Response to Allegations Regarding the Patents In Suit

21. Denied.

22. NanoString admits that, on its face, the 639 Patent states that it was issued on March 12, 2019 and that it lists the named inventors as Daniel Levner, Jehyuk Lee, George M. Church, and Michael Super. Except as so admitted, NanoString denies any remaining allegations of paragraph 22.

23. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 23 and on that basis denies them.

24. NanoString admits that, on its face, the 737 Patent states that it was issued on June 1, 2021 and that it lists the named inventors as Daniel Levner, Jehyuk Lee, George M. Church, and Michael Super. Except as so admitted, NanoString denies any remaining allegations of paragraph 24.

25. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 25 and on that basis denies them.

26. NanoString admits that, on its face, the 051 Patent states that it was issued on April 5, 2022, and that it lists the named inventors as Daniel Levner, Jehyuk Lee, George M. Church, and Michael Super. Except as so admitted, NanoString denies any remaining allegations of paragraph 26.

27. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 27 and on that basis denies them.

28. NanoString admits that, on its face, the 052 Patent states that it was issued on April 5, 2022, and that it lists the named inventors as Daniel Levner, Jehyuk Lee, George M. Church, and Michael Super. Except as so admitted, NanoString denies any remaining allegations of paragraph 28.

29. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 29 and on that basis denies them.

30. NanoString admits that, on its face, the 054 Patent states that it was issued on April 5, 2022, and that it lists the named inventors as Daniel Levner, Jehyuk Lee, George M. Church,

and Michael Super. Except as so admitted, NanoString denies any remaining allegations of paragraph 30.

31. NanoString lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 31 and on that basis denies them.

COUNT I

32. NanoString incorporates and restates by reference its responses to paragraphs 1-31 of the FAC as though fully set forth herein.

33. Denied.

34. Denied.

35. Denied.

COUNT II

36. NanoString incorporates and restates by reference its responses to paragraphs 1-35 of the FAC as though fully set forth herein.

37. Denied.

38. Denied.

39. Denied.

COUNT III

40. NanoString incorporates and restates by reference its responses to paragraphs 1-39 of the FAC as though fully set forth herein.

41. Denied.

42. Denied.

43. Denied.

COUNT IV

44. NanoString incorporates and restates by reference its responses to paragraphs 1-43 of the FAC as though fully set forth herein.

45. Denied.

46. Denied.

47. Denied.

COUNT V

48. NanoString incorporates and restates by reference its responses to paragraphs 1-47 of the FAC as though fully set forth herein.

49. Denied.

50. Denied.

51. Denied.

PRAYER FOR RELIEF

NanoString denies that Plaintiffs are entitled to any relief whatsoever, including the relief stated in paragraphs A through F, from either NanoString or the Court. Plaintiffs' prayer for relief should be denied in its entirety.

AFFIRMATIVE DEFENSES

NanoString hereby sets forth defenses to the FAC in order to place Plaintiffs on notice regarding applicable defenses. By listing any matter as a defense herein, NanoString does not assume the burden of proving any matter upon which Plaintiffs, or any other party, bears the burden of proof under applicable law.

FIRST DEFENSE – NON-INFRINGEMENT

NanoString has not infringed, and is not infringing directly, indirectly, contributorily, by inducement, or in any other manner any valid and enforceable claim of the Asserted Patents, either literally or under the doctrine of equivalents.

SECOND DEFENSE – INVALIDITY

The asserted claims of the Asserted Patents are invalid for failing to comply with one or more of the requirements for patentability under, including, but not limited to 35 U.S.C. §§ 101, 102, 103, 112 et seq., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

THIRD DEFENSE – 35 U.S.C. § 287

Plaintiffs' patent infringement claims and Prayer for Relief are limited by 35 U.S.C. § 287.

FOURTH DEFENSE – ADEQUATE REMEDY AT LAW

Plaintiffs have an adequate remedy at law and the alleged injury to Plaintiffs is not immediate or irreparable. Accordingly, Plaintiffs are not entitled to injunctive relief even if it were able to establish liability.

FIFTH DEFENSE – NO EXCEPTIONAL CASE

NanoString has not engaged in any conduct that would make this an exceptional case or that would entitle Plaintiffs to an award of attorneys' fees.

SIXTH DEFENSE – FAILURE TO STATE A CLAIM

Plaintiffs' FAC fails to state a claim upon which relief may be granted.

NANOSTRING’S AMENDED COUNTERCLAIMS AGAINST PLAINTIFFS

In further response to Plaintiffs’ FAC, Defendant and Counter-Plaintiff NanoString hereby asserts these Counterclaims against Plaintiff Harvard and Counter-Defendant 10x and alleges as follows.

NATURE OF THE ACTION

1. In response to Plaintiffs’ allegations in the FAC, NanoString seeks a declaratory judgment that it has not infringed the Asserted Patents and that the Asserted Patents are invalid, arising under the Patent Laws of the United States 35 U.S.C. § 271 *et seq.* NanoString also seeks a finding of infringement of U.S. Patent No. 11,377,689 (“the ’689 Patent”) by Counter-Defendant 10x.

THE PARTIES

2. Plaintiff 10x is a Delaware corporation with its principal place of business at 6230 Stoneridge Mall Road, Pleasanton, CA 94588.

3. Plaintiff Harvard is a Massachusetts educational institution according to its allegations in the FAC.

4. NanoString is a Delaware corporation with its principal place of business at 530 Fairview Ave. N, Seattle, WA 98109.

JURISDICTION AND VENUE

5. These Counterclaims arise under the Patent Act, and this Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 & 1338, the Declaratory Judgement Act, 28 U.S.C. §§ 2201 & 2202, and the Patent Laws of the United States, 35 U.S.C. § 1, *et seq*

6. The Court has personal jurisdiction over 10x and Harvard because 10x is a Delaware corporation and both 10x and Harvard have consented to jurisdiction in this District by filing their FAC in this action.

7. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391 and 1400(b) because 10x is a Delaware corporation and both 10x and Harvard have consented to this venue by filing their original complaint in this action.

BACKGROUND

8. NanoString is the pioneer in the field of spatial biology. As a respected, leading innovator of translational tools, NanoString has developed and brought to market breakthrough technologies that enable scientists across the globe to envision molecular interactions in three dimensions. NanoString's GeoMx Digital Spatial Profiler ("GeoMx DSP") product is the first of its kind – it uniquely combines high-plex and high-throughput spatial profiling, which allows researchers to rapidly and quantitatively assess the biological implications of heterogeneity within tissues. Since its launch, GeoMx DSP has been amply described in prestigious scientific publications, and studies performed using GeoMx DSP have been widely presented at industry conferences.

9. On July 5, 2022, the United States Patent and Trademark Office duly and legally issued the United States Patent No. 11,377,689 ("the '689 Patent"), entitled "Chemical Compositions and Uses Thereof". The named inventors of the '689 Patent are Joseph Beechem, Dae Kim, Margaret Hoang, Mark Gregory, Erin Piazza, and Denise Zhou. By operation of law and as a result of written assignment agreements, Counterclaim-Plaintiff NanoString obtained the entire right, title, and interest to and in the '689 Patent. The '689 Patent is attached hereto. Ex. 1.

10. Since its issuance, NanoString has owned the '689 Patent.

11. As its Abstract explains, the '689 Patent is directed to an improved and novel way of spatially detecting target analytes in regions of interest. More specifically, the method claimed in the '689 Patent permits the simultaneous, multiplexed detection and quantification of protein

and/or nucleic acid expression in a user-defined region of a tissue, cell, and/or subcellular structure within a cell, while maintaining the morphological context of the sample.

12. The claimed invention of the '689 Patent is an improvement over the prior art means of detecting target analytes in a sample. Conventional immunohistochemical methods allow for simultaneous detection of six to ten protein targets at most. Similarly, *in situ* hybridization methods are limited to less than ten nucleic acid targets. '689 Patent at 16:30-32. While useful, these methods do not enable the simultaneous detection of a large number of genes, proteins, or other biologically active molecules in the same sample. Laser microdissection is able to capture many genes, but it is limited to a small number of locations and very expensive. The claimed invention of the '689 Patent uniquely addresses and solves these problems. As such, the invention offers a spatial profiling method for RNA and/or protein in a tissue sample of much higher plex and sensitivity, providing researchers the ability to look at many biological targets at many locations in the same sample at the same time. As the '689 Patent explains, the "present disclosure provides detection of large combinations of nucleic acid targets and/or protein targets from a defined region of a sample. The present disclosure provides an increase in objective measurements by digital quantification and increased reliability and consistency, thereby enabling comparison of results among multiple centers." *Id.* at 16:37-43. Specifically, more than 1000 targets can be detected, and "[t]here is no pre-defined upper limit to the number of regions of interest and comparisons that can be made." *Id.* at 16:21-23; 40:61-64. Furthermore, the invention is compatible with existing, readily available sequencing technologies, making it accessible to a large number of users; it also allows for an economical assay design, as inexpensive and widely-available synthetic DNA oligonucleotides can be used instead of more expensive probes. *Id.* at Abstract; 37:50-55.

13. On information and belief, 10x launched and began shipping its commercial spatial profiling products, Visium Spatial system (“Visium”) and related products in November, 2019.

See <https://www.globenewswire.com/news-release/2019/11/26/1952684/0/en/10x-Genomics-Begins-Shipments-of-Visium-Spatial-Gene-Expression-Solution.html>.

14. Visium and related products are all products, components, and services that are made, used, performed, offered to sell, sold, and/or imported in the United States by or on behalf of 10x in connection with 10x’s Visium. Visium and related products include, for example and without limitation, Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization software, Space Ranger and Loupe Browser, and Certified Service Providers (CSP), that when used together allow researchers to “map the whole transcriptome within the tissue context” and “[c]ombine histological and gene expression data with easy-to-use software.” See <https://www.10xgenomics.com/products/spatial-gene-expression>.

15. Visium and related products provide spatial profiling for protein and/or RNA in a tissue sample. 10x offers benchtop instrument, slides, reagents, and software for protein and RNA analysis using workflows that are compatible with standard next generation sequencing (NGS) applications. 10x markets Visium as designed to “discover and reveal the spatial organization of cell types, states, and biomarkers.” See https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT059_ProductSheet_VisiumSpatialGeneExpression_Letter_digital.pdf.

Furthermore, 10x states that Visium is able to “[s]patially profile RNA expression for over 18,000 genes in human and mouse FFPE samples with high resolution across entire tissue sections,” see https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT000128_PS_Spatial_biology_without_limits_Spatial_gene_expression_in_F

[FPE.pdf](#), offers “tissue profiling with transcriptomics and protein co-detection,” *see* <https://www.10xgenomics.com/products/spatial-proteogenomics>, allows users to “define regions of interest,” *see* https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT088_RevA_ProductSheet_Immunofluorescence%20Capability_Letter_digit_al.pdf, and is “[e]asy to integrate with current histological laboratory methods and tools for tissue analysis.” *Id.*

16. 10x practices the ’689 Patent by using Visium and related products on behalf of its own scientists, researchers, and its Visium customers for various purposes, including without limitation research, development, sales, and support.

17. 10x infringes the ’689 Patent by providing customers with Certified Service Providers (CSP), who offer support for complete end-to-end Visium workflows and perform various tasks, from sample preparation to library generation to data processing, for its customers. *See* <https://www.10xgenomics.com/service-providers?query=&page=1>.

18. 10x additionally infringes the ’689 Patent by making, using, selling, offering for sale, importing into the United States, and supplying from the United States the patented inventions and/or its components, including without limitation Visium, Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization software, Space Ranger and Loupe Browser, and CSP.

19. Through the development and subsequent making, using, selling, offering for sale, importing and exporting of its Visium and related products, and performing every step of the patented invention by using products, services, devices, systems, and/or components of the systems that embody the patented inventions, such as Visium and related products, 10x has and

continues to directly infringe, contributorily infringe, and/or induce the infringement of the '689 Patent.

FIRST COUNT

(Declaration of Non-Infringement of United States Patent No. 10,227,639)

20. NanoString incorporates by references and restates the preceding Paragraphs 1-18 of its Counterclaims as though fully set forth herein.

21. Plaintiffs have brought an action asserting the 639 Patent against NanoString.

22. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 639 Patent.

23. Plaintiff 10x has alleged that it is the exclusive licensee of the 639 Patent.

24. Plaintiffs have alleged and continue to allege that NanoString has infringed and continues to infringe one or more claims of the 639 Patent.

25. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 639 Patent.

26. NanoString's products are not infringing directly or in any other manner any valid and enforceable claim of the 639 Patent.

27. For example, as described therein, when properly construed, the 639 Patent claims require analytes to be immobilized in the sample for analyte identification. In contrast, NanoString's CosMx SMI does not immobilize analytes for analyte identification.

28. Also, as described therein, when properly construed, the 639 Patent claims require pre-determined subsequences to form an identifier of analyte. In contrast, to the extent they are used in CosMx SMI, pre-determined subsequences are not identifiers, but intermediate sequences for hybridization of probes.

29. Furthermore, as described therein, when properly construed, the 639 Patent claims require a first decoder probe to be removed before the hybridization of the second decoder probe. In contrast, CosMx SMI do not remove any such decoder probes during hybridization.

30. Moreover, as described therein, when properly construed, the 639 Patent claims require identification of a probe for analyte identification. In contrast, NanoString's CosMx SMI does not identify a probe to identify an analyte.

31. Besides, as described therein, when properly construed, the 639 Patent claims require the use of two detectable labels for analyte identification. To the extent any accused products do not use two detectable labels for analyte identification, they do not infringe the 639 Patent.

32. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 639 Patent.

33. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

SECOND COUNT

(Declaration of Non-Infringement of United States Patent No. 11,021,737)

34. NanoString incorporates by references and restates the preceding Paragraphs 1-32 of its Counterclaims as though fully set forth herein.

35. Plaintiffs have brought an action asserting the 737 Patent against NanoString.

36. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 737 Patent.

37. Plaintiff 10x has alleged that it is the exclusive licensee of the 737 Patent.

38. Plaintiffs have alleged and continue to allege that NanoString has infringed and continues to infringe one or more claims of the 737 Patent.

39. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 737 Patent.

40. NanoString's products are not infringing directly or in any other manner any valid and enforceable claim of the 737 Patent.

41. For example, as described therein, when properly construed, the 737 Patent claims require the analytes to be in the cell or tissue sample during analyte identification. In contrast, NanoString's CosMx SMI does not identify analytes in the cell or tissue sample.

42. Furthermore, as described therein, when properly construed, the 737 Patent claims require signal signatures to be associated with one or more pre-determined subsequences. In contrast, to the extent they are used in CosMx SMI, signal signatures are not associated with pre-determined subsequences, but with the hybridized decoder probes.

43. Moreover, as described therein, when properly construed, the 737 Patent claims require first decoder probe to be removed before the hybridization of the second decoder probe. In contrast, CosMx SMI does not remove the decoder probes during serial hybridization.

44. Besides, as described therein, when properly construed, the 737 Patent require a temporal order of signal signatures for analyte identification. To the extent any accused products do not use a temporal order of signal signatures for analyte identification, they do not infringe the 639 Patent.

45. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 737 Patent.

46. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

THIRD COUNT

(Declaration of Non-Infringement of United States Patent No. 11,293,051)

47. NanoString incorporates by references and restates the preceding Paragraphs 1-45 of its Counterclaims as though fully set forth herein.

48. Plaintiffs have brought an action asserting the 051 Patent against NanoString.

49. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 051 Patent.

50. Plaintiff 10x has alleged that it is the exclusive licensee of the 051 Patent.

51. Plaintiffs have alleged and continue to allege that NanoString has infringed and continues to infringe one or more claims of the 051 Patent.

52. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 051 Patent.

53. NanoString's products are not infringing directly or in any other manner any valid and enforceable claim of the 051 Patent.

54. For example, as described therein, when properly construed, the 051 Patent claims require the analytes to be in the cell or tissue sample for analyte identification. In contrast, NanoString's CosMx SMI does not identify analytes in the cell or tissue sample.

55. Also, as described therein, when properly construed, the 051 Patent claims require a temporal order of signal signatures to correspond to a location in a cell or tissue sample. In contrast, NanoString's CosMx SMI does not use a temporal order of signal signatures corresponding to a location.

56. Furthermore, as described therein, when properly construed, the 051 Patent claims require first plurality of signal signatures to be removed from the cell or tissue sample before the

second readout cycle. In contrast, CosMx SMI does not remove the first signal signatures from the cell or tissue sample, but from the bound probes.

57. Moreover, as described therein, when properly construed, the 051 Patent claims require the first subset of detection reagents associated with the first set of decoding reagents and the second set of detection reagents associated with the second set of decoding reagents to overlap. To the extent any of the accused products do not let the first subset of detection reagents and the second subset of detection reagents to overlap, they do not infringe the 051 Patent.

58. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 051 Patent.

59. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

FOURTH COUNT

(Declaration of Non-Infringement of United States Patent No. 11,293,052)

60. NanoString incorporates by references and restates the preceding Paragraphs 1-58 of its Counterclaims as though fully set forth herein.

61. Plaintiffs have brought an action asserting the 052 Patent against NanoString.

62. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 052 Patent.

63. Plaintiff 10x has alleged that it is the exclusive licensee of the 052 Patent.

64. Plaintiffs have alleged and continue to allege that NanoString has infringed and continues to infringe one or more claims of the 052 Patent.

65. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 052 Patent.

66. NanoString's products are not infringing directly or in any other manner any valid and enforceable claim of the 052 Patent.

67. For example, as described therein, when properly construed, the 052 Patent claims require the analyte to be at a location in a biological sample during identification. In contrast, NanoString's CosMx SMI does not identify the analyte at the location in a biological sample.

68. Furthermore, as described therein, when properly construed, the 052 Patent claims require the first optical signal to be removed from the location in the biological sample before the second readout cycle. In contrast, CosMx SMI does not remove the first optical signal from the sample, but from the bound probes.

69. Moreover, as described therein, when properly construed, the 052 Patent claims require the detection of multiple signal signatures and the absence thereof during analyte identification. To the extent any of the accused products do not detect multiple signal signatures for analyte detection, they do not infringe the 052 Patent.

70. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 052 Patent.

71. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

FIFTH COUNT

(Declaration of Non-Infringement of United States Patent No. 11,293,054)

72. NanoString incorporates by references and restates the preceding Paragraphs 1-70 of its Counterclaims as though fully set forth herein.

73. Plaintiffs have brought an action asserting the 054 Patent against NanoString.

74. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 054 Patent.

75. Plaintiff 10x has alleged that it is the exclusive licensee of the 054 Patent.

76. Plaintiffs have alleged and continue to allege that NanoString has infringed and continues to infringe one or more claims of the 054 Patent.

77. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 054 Patent.

78. NanoString's products are not infringing directly or in any other manner any valid and enforceable claim of the 054 Patent.

79. For example, as described therein, when properly construed, the 054 Patent claims require generation of signal signatures in a cell or tissue sample. In contrast, NanoString's CosMx SMI does not generate a signal signatures in a cell or tissue sample.

80. Furthermore, as described therein, when properly construed, the 054 Patent claims require a nucleic acid label coupled to a probe to permit the said probe to bind to an analyte. In contrast, to the extent it is used in NanoString's CosMx SMI, the nucleic acid label does not permit the probe to bind to an analyte. Rather, the probe is itself designed to target an analyte.

81. Moreover, as described therein, when properly construed, the 054 Patent claims require first decoder probe to be removed before the hybridization of the second decoder probe. In contrast, CosMx SMI do not remove the decoder probes during serial hybridization.

82. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 054 Patent.

83. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

SIXTH COUNT

(Declaration of Invalidity of U.S. Patent No. 10,227,639)

84. NanoString incorporates by references and restates the preceding Paragraphs 1-82 of its Counterclaims as though fully set forth herein.

85. Plaintiffs have brought an action asserting the 639 Patent against NanoString.

86. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 639 Patent.

87. Plaintiff 10x has alleged that it is the exclusive license of the 639 Patent.

88. Plaintiffs have alleged and continues to allege that NanoString has infringed and continues to infringe one or more claims of the 639 Patent.

89. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 639 Patent.

90. The claims of the 639 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations and law pertaining thereto.

91. For example, the asserted claims of the Asserted Patents are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of U.S. Patent No. 10,961,566 (“Chee”), alone or in combination with additional prior art, including U.S. Patent App. Pub. No. 2005/0064435 (“Su”), Göransson et al., A single molecule array for digital targeted molecular analyses, 37 Nucleic Acids Research e7 (2008) (“Göransson”), or U.S. Patent No. 8,741,566 (“Winther”), which disclose and/or render obvious all elements of the claims of the Asserted Patents.

92. All claims of the Asserted Patents are further invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the claim term “temporal order”, read in light of

the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art of the boundaries of protected subject matter, and therefore does not meet the definiteness standard.

93. Moreover, the specifications of the Asserted Patents fail to contain a written description of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of an adequate written description and a lack of enablement for signal detection in the cell or tissue sample.

94. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 639 Patent.

95. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

SEVENTH COUNT

(Declaration of Invalidity of U.S. Patent No. 11,021,737)

96. NanoString incorporates by references and restates the preceding Paragraphs 1-94 of its Counterclaims as though fully set forth herein.

97. Plaintiffs have brought an action asserting the 737 Patent against NanoString.

98. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 737 Patent.

99. Plaintiff 10x has alleged that it is the exclusive license of the 737 Patent.

100. Plaintiffs have alleged and continues to allege that NanoString has infringed and continues to infringe one or more claims of the 737 Patent.

101. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 737 Patent.

102. The claims of the 737 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations and law pertaining thereto.

103. For example, the asserted claims of the Asserted Patents are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of U.S. Patent No. 10,961,566 (“Chee”), alone or in combination with additional prior art, including U.S. Patent App. Pub. No. 2005/0064435 (“Su”), Göransson et al., A single molecule array for digital targeted molecular analyses, 37 Nucleic Acids Research e7 (2008) (“Göransson”), or U.S. Patent No. 8,741,566 (“Winther”), which disclose and/or render obvious all elements of the claims of the Asserted Patents.

104. All claims of the Asserted Patents are further invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the claim term “temporal order”, read in light of the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art of the boundaries of protected subject matter, and therefore does not meet the definiteness standard.

105. Moreover, the specifications of the Asserted Patents fail to contain a written description of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of an adequate written description and a lack of enablement for generating a three dimensional matrix of nucleic acids in situ in a cell or tissue sample and amplifying, detecting, and sequencing such nucleic acids within the matrix; there is also a lack of an adequate written description and a lack of enablement for analyte detection while allowing spatial movement of an analyte in a sample.

106. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 737 Patent.

107. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

EIGHTH COUNT

(Declaration of Invalidity of U.S. Patent No. 11,293,051)

108. NanoString incorporates by references and restates the preceding Paragraphs 1-106 of its Counterclaims as though fully set forth herein.

109. Plaintiffs have brought an action asserting the 051 Patent against NanoString.

110. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 051 Patent.

111. Plaintiff 10x has alleged that it is the exclusive license of the 051 Patent.

112. Plaintiffs have alleged and continues to allege that NanoString has infringed and continues to infringe one or more claims of the 051 Patent.

113. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 051 Patent.

114. The claims of the 051 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations and law pertaining thereto.

115. For example, the asserted claims of the Asserted Patents are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of U.S. Patent No. 10,961,566 (“Chee”), alone or in combination with additional prior art, including U.S. Patent App. Pub. No. 2005/0064435 (“Su”), Göransson et

al., A single molecule array for digital targeted molecular analyses, 37 Nucleic Acids Research e7 (2008) (“Göransson”), or U.S. Patent No. 8,741,566 (“Winther”), which disclose and/or render obvious all elements of the claims of the Asserted Patents.

116. Moreover, the specifications of the Asserted Patents fail to contain a written description of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of an adequate written description and a lack of enablement for generating a three dimensional matrix of nucleic acids in situ in a cell or tissue sample and amplifying, detecting, and sequencing such nucleic acids within the matrix; there is also a lack of an adequate written description and a lack of enablement for analyte detection while allowing spatial movement of an analyte in a sample.

117. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 051 Patent.

118. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

NINTH COUNT

(Declaration of Invalidity of U.S. Patent No. 11,293,052)

119. NanoString incorporates by references and restates the preceding Paragraphs 1-117 of its Counterclaims as though fully set forth herein.

120. Plaintiffs have brought an action asserting the 052 Patent against NanoString.

121. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 052 Patent.

122. Plaintiff 10x has alleged that it is the exclusive license of the 052 Patent.

123. Plaintiffs have alleged and continues to allege that NanoString has infringed and continues to infringe one or more claims of the 052 Patent.

124. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 052 Patent.

125. The claims of the 052 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations and law pertaining thereto.

126. For example, the asserted claims of the Asserted Patents are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of U.S. Patent No. 10,961,566 (“Chee”), alone or in combination with additional prior art, including U.S. Patent App. Pub. No. 2005/0064435 (“Su”), Göransson et al., A single molecule array for digital targeted molecular analyses, 37 Nucleic Acids Research e7 (2008) (“Göransson”), or U.S. Patent No. 8,741,566 (“Winther”), which disclose and/or render obvious all elements of the claims of the Asserted Patents.

127. All claims of the Asserted Patents are further invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the claim terms “signal signature” and “temporal order”, read in light of the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art of the boundaries of protected subject matter, and therefore does not meet the definiteness standard.

128. Moreover, the specifications of the Asserted Patents fail to contain a written description of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of an adequate written description and a lack of enablement for analyte identification at a location in a biological sample.

129. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 052 Patent.

130. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

TENTH COUNT

(Declaration of Invalidity of U.S. Patent No. 11,293,054)

131. NanoString incorporates by references and restates the preceding Paragraphs 1-129 of its Counterclaims as though fully set forth herein.

132. Plaintiffs have brought an action asserting the 054 Patent against NanoString.

133. Plaintiff Harvard has alleged that it is the legal owner by assignment of the 054 Patent.

134. Plaintiff 10x has alleged that it is the exclusive license of the 054 Patent.

135. Plaintiffs have alleged and continues to allege that NanoString has infringed and continues to infringe one or more claims of the 054 Patent.

136. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Plaintiffs and NanoString concerning whether NanoString has infringed and is infringing any valid and enforceable claim of the 054 Patent.

137. The claims of the 054 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations and law pertaining thereto.

138. For example, the asserted claims of the Asserted Patents are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of U.S. Patent No. 10,961,566 (“Chee”), alone or in combination with additional prior art, including U.S. Patent App. Pub. No. 2005/0064435 (“Su”), Göransson et

al., A single molecule array for digital targeted molecular analyses, 37 Nucleic Acids Research e7 (2008) (“Göransson”), or U.S. Patent No. 8,741,566 (“Winther”), which disclose and/or render obvious all elements of the claims of the Asserted Patents.

139. All claims of the Asserted Patents are further invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the claim term “temporal order”, read in light of the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art of the boundaries of protected subject matter, and therefore does not meet the definiteness standard.

140. Moreover, the specifications of the Asserted Patents fail to contain a written description of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of an adequate written description and a lack of enablement for signal detection in the cell or tissue sample.

141. By virtue of the foregoing, NanoString desires a judicial determination of its rights and duties with respect to any alleged infringement of the 054 Patent.

142. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

ELEVENTH COUNT

(Infringement of United States Patent No. 11,377,689 by 10x)

143. NanoString incorporates by references and restates the preceding Paragraphs 141 of its Counterclaims as though fully set forth herein.

144. 10x has infringed and continues to directly infringe one or more claims of the ’689 Patent, including without limitation claims 1-30, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority all products, components, and services in connection with

10x's Visium, including without limitation Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization software, Space Ranger and Loupe Browser, CSP, and other products and services sold by 10x for use in 10x's Visium workflows.

145. 10x has had knowledge of the '689 Patent since at least July 11, 2022, the date when 10x was notified of NanoString's intent to add a counterclaim of infringement of U.S. Patent 11,377,689 to the 22-cv-261 litigation. Furthermore, 10x received NanoString's proposed amended counterclaims, along with detailed infringement claim chart applying the '689 Patent to 10x's products, on July 19, 2022. On information and belief, 10x's outside counsel subsequently reviewed NanoString's amended pleadings with 10x's internal legal personnel, and 10x has affirmatively decided to continue infringing. At the very least, service of NanoString's proposed amended counterclaim on July 19, 2022 provided 10x with not just notice of the '689 Patent, but also 10x's ongoing infringement of the '689 patent. 10x's infringement since this time has been willful.

146. 10x has actively induced and continues to induce the infringement of one or more claims of the '689 Patent, including without limitation claims 1-30, pursuant to 35 U.S.C. § 271(b) through a range of activities, including without limitation making and selling Visium and related products; controlling the design, manufacture, and supply of materials, software, and instruments to be used with Visium and related products; substantially marketing Visium and related products; intentionally instructing or otherwise encouraging others, including 10x's customers and end users, to use the infringing products in the United States in the manner that infringes one or more claims of the '689 Patent; creating distribution channels for the infringing products; and supporting the sale of those products in the United States. As an example, 10x implemented Certified Service

Provider (CSP) program to promote, service, and sell the infringing products domestically. As a further example, 10x distributes Visium and related products promotional and marketing materials and Visium and related products User Manuals in websites directed to the United States Market.

147. 10x has contributed and continues to contribute to the infringement of one or more claims of the '689 Patent, including without limitation claims 1-30, pursuant to 35 U.S.C. § 271(c) through a range of activities, including without limitation, without authority, importing into the United States materials and instruments that are material components of the claimed inventions of the '689 Patent; without authority, importing into the United States materials and instruments for practicing the patented method of the '689 Patent; selling and/or offering for sale Visium and related products, or has others perform such acts on its behalf; and instructing users of 10x's Visium workflows to directly infringe one or more claims of the '689 Patent. Visium and related products are specifically designed to be used in an infringing manner, where no non-infringing use of Visium and related products has been described in 10x's instructional materials. Therefore, 10x's Visium and related products constitute a material part of the claimed invention of the '689 Patent, and are not a staple article or commodity of commerce suitable for substantial non-infringing use. As an example, 10x supplies in the United States products specifically designed for use in practicing one or more claims of the '689 Patent, including for example the Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, Space Ranger, and Loupe Browser and threaten to sell those products throughout the United States.

148. To demonstrate how 10x infringes one or more claims of the '689 Patent, attached is a preliminary and exemplary infringement claim chart. Ex. 2. This chart is not intended to limit NanoString's right to modify this chart or any other claim chart or allege that other activities of 10x infringes the identified claims or any other claims of the '689 Patent or any other patents. This

chart is hereby incorporated by reference in its entirety. Each claim element that is mapped to Visium and related products shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

149. NanoString has suffered and continues to suffer damages as a result of 10x's infringement of the '689 Patent.

150. Unless 10x is enjoined from infringing the '689 Patent, 10x's efforts to design, develop, market, offer to sell, and sell Visium and related products will cause NanoString to suffer irreparable injury for which damages are an inadequate remedy.

REQUEST FOR RELIEF

WHEREFORE, having fully answered Plaintiffs' FAC and having asserted Affirmative Defenses, and Counterclaims, NanoString respectfully requests the following relief:

A. That this Court enter judgment on Plaintiffs' FAC and NanoString's Counterclaims in favor of NanoString, against Plaintiffs, with Plaintiffs being awarded no relief of any kind in this action;

B. That this Court enter judgment and/or declarations that NanoString does not infringe the Asserted Patents and that the Asserted Patents are invalid;

C. That this Court enter judgement that Counterclaim-Defendant 10x has infringed and continues to infringe one or more claims of the '689 Patent, either literally or under the doctrine of equivalents;

D. That this Court enter a declaration that the '689 Patent is valid and enforceable;

E. That this Court enter an order preliminarily and permanently enjoining Counterclaims-Defendant 10x, and its officers, directors, agents, servants, affiliates, employees, divisions, branches, subsidiaries, parents, assigns and successors in interest, and all others acting in active concert therewith, including related individuals and entities, customers, representatives,

distributors, and dealers, from further infringement of the '689 Patent. In the alternative, if the Court finds that an injunction is not warranted, Counterclaim-Plaintiff NanoString requests an award of post-judgement royalty to compensate for future infringement;

F. An award of all monetary relief adequate to compensate for damages resulting from 10x's infringement, including lost profits but in no event less than a reasonable royalty under 35 U.S.C. § 284 for 10x's infringement, including all pre-judgment and post-judgment interest at the maximum rate allowed by law;

G. That this Court enter a judgment declaring this case exceptional under 35 U.S.C. § 285 and awarding NanoString its attorneys' fees and prejudgment and post-judgment interest;H.

That this Court award NanoString all of its costs of this action; and

I. That this Court grant such other and further relief as the Court shall deem just and proper.

Respectfully submitted,
FARNAN LLP

OF COUNSEL:

Edward R. Reines
Derek C. Walter
WEIL, GOTSHAL & MANGES LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
(650) 802-3000

By: /s/ Brian E. Farnan
Brian E. Farnan (Bar No. 4089)
Michael J. Farnan (Bar No. 5165)
919 N. Market St., 12th Floor
Wilmington, DE 19801
(302) 777-0300
(302) 777-0301 (Fax)
bfarnan@farnanlaw.com
mfarnan@farnanlaw.com

*Attorneys for Defendant
Nanostring Technologies, Inc.*

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